

Changes in the Localization of Perforated Peptic Ulcer and its Relation to Gender and Age of the Patients throughout the Last 45 Years

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Abstract

Background Throughout recent decades there has been noticeable change in the incidence of peptic ulcer disease and its complications. The aim of the present study was to determine the character of changes over the last 45 years in the localization of perforation, in patient age, and in patient gender.

Methods A group of 881 patients admitted to the Second Department of General Surgery in Krakow, Poland, from 1962 to 2006 were included in the study and constituted the material for the analysis. The study was divided into three time periods (1962–1976, 1977–1991, and 1992–2006) to allow statistical analysis of trends.

Results The general incidence of perforations of peptic ulcer did not show changes; however, the percentage of women with perforated duodenal ulcer markedly increased. Patients with perforated stomach ulcer—regardless of gender—and females suffering from perforated duodenal ulcer were, on the average, about 10 years older than males with perforated duodenal ulcers. The mean age of male and female patients with perforated duodenal ulcer over the last 45 years showed an insignificant upward trend.

Conclusions (1) The percentage of women with perforated duodenal ulcer continuously and statistically significantly rose. (2) Men with perforated duodenal ulcer were significantly younger than other patients. (3) The mean ages of male and female patients with perforated duodenal ulcer over the last 45 years showed an insignificant upward trend.

Introduction

Epidemiological research on uncomplicated peptic ulcer disease is methodically difficult and thus not free from mistakes. One of the causes of such a situation is a diverse clinical course of peptic ulcer disease, with mutable intensity of complaints and the presence of interweaving periods of relapse and remissions of different duration. Another problem results from changes in the diagnostic workup confirming peptic ulcer that evolved from clinical assessment alone, through radiological examination, to gastroscopy, which nowadays constitutes the diagnostic method of choice. Altogether, these are the reasons for difficulty in comparing the present incidence of the disease with the morbidity recorded in the past. Another problem affecting the precision of epidemiological research is the presence of still-improving pharmaceutical agents that have led to a marked decrease in the number of patients hospitalized for the treatment of peptic ulcer. Moreover, there is still a large group of young patients being treated only on the basis of clinical assessment, without gastroscopy confirming the ulcer and its location [1–6].

The situation is different in cases of complications of peptic ulcer disease that usually cause severe complaints and constitute an indication for hospitalization. Similarly, in cases of bleeding ulcer and stenosis of the gastric outlet, the complaints usually lead to hospitalization. Nevertheless, both diagnostic and therapeutic approaches have changed so much during the last half century that present observations cannot be compared with previous ones.

Perforation of peptic ulcer constitutes a unique situation characterized by severe pain, leading almost every patient with this complication to seek help in the hospital. On the basis of criteria that have remained invariable for decades, such patients are, as a rule, treated surgically, and that not

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only allows for verification of the diagnosis but also for the precise localization of the ulcer as well, thus making possible comparison of data collected over many years.

Determination of changes in the localization of perforated peptic ulcer and variations in gender and age of the patients over the last 45 years constituted the aim of the present study.

Materials and methods

Between 1 January 1962 and 31 December 2006, 871 patients underwent operation for perforated peptic ulcer in the Second Department of General Surgery of Jagiellonian University Medical College in Krakow. In another ten patients admitted in a terminal state, the diagnosis of perforation was made at autopsy. In the whole group of 881 patients included in the study, there were 776 cases of perforated duodenal ulcer and 105 cases of perforated stomach ulcer. There were 672 male and 209 female patients.

Our referral population was not demographically constant for the whole 45 years of the study period. However, with the increase in the head count of the population of Krakow came the foundation of new hospitals admitting acute surgical cases in the same area. Thus the number of patients with acute surgical diseases treated in the Second Department of General Surgery of Jagiellonian University Medical College in Krakow remained on comparable level until 2002. Differences in the incidence of gastric ulcer calculated for this population did not differ significantly. In women the incidence increased from 0.8 to 1.2/100,000/year, whereas, in men, the incidence decreased from 3.4 to 2.3. Simultaneously the incidence of duodenal ulcer in the male population decreased from 29.6 to 22.7 (difference insignificant statistically), whereas in the female population it increased significantly from 3.5 to 9.4. Unfortunately, because of some more pronounced changes in the referral population and the structure of the medical service from 2003 to the present, we were not able to calculate the exact incidence and present it in our study. The observation time of 45 years was divided into three periods: 1962–1976 (15 years), 1977–1991 (15 years), and 1992–2006 (15 years). Calculations were made separately for each gender and for stomach ulcers and duodenal ulcers. Student's *t* test and the χ^2 test were used in statistical assessment.

Results

Localization

Throughout the 45-year observation time, perforation of duodenal ulcer proved to be more than seven times more

frequent than perforation of stomach ulcer when calculated together for both sexes. Differences among particular periods of the study were slight and did not show statistical significance (Table 1).

Gender

There was an increase in the percentage of women in the group of patients with perforated duodenal ulcer observed in consecutive periods of the study (Table 2). Differences in the proportion of female patients between the third and the second periods and between the third and the first periods were statistically significant ($P < 0.01$). An increase in the percentage of women between the first and the second periods also proved significant ($P < 0.05$).

There were no statistically significant differences observed in gender distribution of perforated gastric ulcer (Table 3).

Table 1 Localization of perforated peptic ulcer

Period	Duodenal ulcer <i>n</i> (%)	Stomach ulcer <i>n</i> (%)	Together <i>n</i>
I (1962–1976)	227 (87.6)	21 (12.4) ^a	259
II (1977–1991)	249 (86.5)	39 (13.5) ^b	288
III (1992–2006)	300 (89.8)	34 (10.2) ^c	334
I + II + III	776 (88.1)	105 (11.9)	881

a/b, *a/c*, and *b/c* differences without statistical significance

Table 2 Gender differences in perforated duodenal ulcer

Period	Male patients <i>n</i> (%)	Female patients <i>n</i> (%)	Together <i>n</i>
I (1962–1976)	199 (87.7)	28 (12.3) ^a	227
II (1977–1991)	200 (80.3)	49 (19.7) ^b	249
III (1992–2006)	203 (67.7)	97 (32.3) ^c	300
I + II + III	602 (77.6)	174 (22.4)	776

a/b difference with statistical significance ($P < 0.05$)

a/c and *b/c* differences with statistical significance ($P < 0.01$)

Table 3 Gender differences in perforated stomach ulcer

Period	Male patients <i>n</i> (%)	Female patients <i>n</i> (%)	Together <i>n</i>
I (1962–1976)	21 (65.6)	11 (34.4) ^a	32
II (1977–1991)	27 (69.2)	12 (30.8) ^b	39
III (1992–2006)	22 (64.7)	12 (35.3) ^c	34
I + II + III	70 (66.7)	35 (33.3)	105

a/b, *a/c*, and *b/c* differences without statistical significance

Age

Mean ages of both male and female patients with perforated duodenal ulcer presented an upward trend; however, that trend was without statistical significance (Tables 4, 5). The mean age of the female patients in every period of the study (a/d, b/e, c/f and for the study as a whole) was significantly higher than mean age of the male patients at $P < 0.001$. Mean ages for both sexes showed an upward trend; however, this regularity did not prove to be statistically significant.

Only the mean age of women with perforated stomach ulcer in the third period (a/b in Table 5) was significantly higher than in the second period ($P < 0.05$). Otherwise, changes in the age of male and female patients did not show statistical significance. Mean age of female patients—except for the second period—was insignificantly higher than the mean age of male patients, although the mean age of men showed an upward trend.

Men with perforated stomach ulcer were significantly older than men with duodenal ulcer at $P < 0.05$ for the first and the third periods, and at $P < 0.001$ for the second period. Women with perforated stomach ulcer were only 2 years older than women with duodenal ulcer, and this difference showed no significance, either for the whole group or for particular periods.

For whole study period women with perforated duodenal ulcer were more than 12 years older than men ($P < 0.001$). Mean ages of female patients with duodenal and stomach ulcers were similar. The 9-year difference between the groups of male patients with duodenal and

stomach ulcers proved to be statistically significant ($P < 0.01$). In the group of patients with perforated stomach ulcer, women were more than 6 years older than men, but this difference proved insignificant.

Discussion

Jan Mikulicz Radecki, professor of surgery at Jagiellonian University at that time, was mentioned in the literature as the first surgeon who had sutured a perforated ulcer [7]. This statement requires correction—in 1885, during the Congress of Naturalists in Magdeburg, Radecki presented the case of a patient he had operated on in Theodor Billroth's department in Vienna. Precise description of the case includes a 7-cm-long subcardial rupture of the gastric wall and not a perforated ulcer. The lecture was published in the same year in a Cracovian paper titled “Przegląd Lekarski” [8]. Ludwik Heuser in Wuppertal and Hastings Gilford in England in 1892 were truly the first surgeons who successfully closed perforated ulcers [9].

Age and gender of the patients and localization of perforation have changed over the years. For example in the middle of the nineteenth century in England perforation in the subcardial region dominated, with young women being the most commonly affected group of patients [10]. In recent years there has been a marked change in the incidence of peptic ulcer disease observed in many countries [5, 6, 11–14]. Starting in the 1980s there has been a marked decrease in the number of hospitalizations due to peptic ulcer disease. This change is related to the introduction of modern pharmacotherapy, initially based on H_2 -blockers, and later modified (with the use of proton pump inhibitors [PPIs], which were introduced in 1988) and supplemented with the use of eradication of *Helicobacter pylori* [5, 6, 14–18]. The decrease in hospitalizations was also a result of ambulatory treatment of uncomplicated peptic ulcer disease. However, despite the use of more and more effective drugs, there was not a comparable decrease in the number of complications of this disease [6, 14, 16, 18, 19]. In fact, the incidence of complications such as hemorrhage and perforation has fluctuated for years, and marked differences were observed among the various countries and time periods reported [11, 13, 15, 16, 20–27]. Along with the downward trend in perforations observed in Europe, there was marked increase in the number of perforations observed elsewhere—e.g., in Hong-Kong [14, 21, 24, 26, 27]. Even within a single country there were significant differences between regions (even those close to one another) [20]. Causes of such observations cannot be unequivocally explained; however, the literature suggests a role for changes in dietary customs, smoking habits, and a continuing increase in the use of non-steroidal anti-inflammatory drugs (NSAIDs) [3, 28–31].

Table 4 Mean age of patients with perforated duodenal ulcer

Period	Male patients age, years (SD)	Female patients age, years (SD)
I (1962–1976)	44.5 (16.4) ^a	55.04 (13.98) ^d
II (1977–1991)	45.8 (17.1) ^b	57.7 (20.7) ^c
III (1992–2006)	47.2 (16.2) ^c	60.6 (18.97) ^f
I + II + III	45.85 (16.6)	58.89 (18.8)

a/d, b/e, c/f and for whole study group differences with statistical significance ($P < 0.001$)

Table 5 Mean age of patients with perforated stomach ulcer

Period	Male patients age, years (SD)	Female patients age, years (SD)
I (1962–1976)	51.1 (12.8)	59.5 (21.6)
II (1977–1991)	57.6 (12.7)	54.25 (17.05) ^a
III (1992–2006)	56.95 (15.8) ^c	69.25 (17.9) ^b
I + II + III	55.47 (13.86)	61.06 (19.39)

a/b difference with statistical significance ($P < 0.05$)

Differences concern the general incidence of ulcer and its changes in time, gender proportion, localization of the ulcer and, finally, the age of the patients [5, 21, 27, 30, 32–35]. Changes in the number of perforations in consecutive decades can be explained by the fact that cohorts of people born at the beginning of the twentieth century were more likely to suffer from perforation than people born later [36]. This statement is confirmed by the epidemiological observations of the population of Iceland, which represents a closed population that does not undergo marked fluctuations. Those studies confirmed the highest risk of perforation in the group of people born during the first and the second decades of the twentieth century. In Iceland those generations had the highest prevalence of *H. pylori* antibodies [37].

Nowadays perforations of duodenal ulcer are found mostly in men; however, there has been an increase in the proportion of women [13, 15, 17–19, 38]. Such a trend was also observed in the second half of the twentieth century in Norway [36]. In many studies, coming mostly from Great Britain, authors pay attention to the decrease in the number of ulcer perforations with the concomitant increase in the proportion of elderly women suffering from this complication [15, 17, 18, 26, 27, 32, 33, 39, 40]. Those changes are related to different factors, including among others, dietary habits (difficult to confirm), including alcohol use. Smoking also seems to play an important role as a causative factor [18, 22, 39, 41]. However, the incidence of ulcer perforations is influenced the most by the use of NSAIDs, which increase the risk of perforation 6–8 times [11, 13, 22, 39, 41, 42]. The use of NSAIDs among older women is widespread and still rising, confirming strong relationship between the use of NSAIDs and the incidence of complications of peptic ulcer disease [13, 22, 27–29, 43]. *Helicobacter pylori* infection—so important in the pathogenesis of uncomplicated peptic ulcer disease—did not prove to play an important role in perforations. In some studies the percentage of infected patients in the group suffering from perforation amounted to about 20% [39]. Other studies, however, found a low percentage of patients infected with *H. pylori* only in the group of people taking NSAIDs, whereas in the remaining patients the incidence of *H. pylori* infection was similar to the group of uncomplicated peptic ulcer disease [44, 45]. The abovementioned epidemiological study from Iceland also indicates the important role of *H. pylori* infection [37]. It seems that marked differences in the percentage of patients with perforated peptic ulcer infected by *H. pylori* can result from the way in which this infection is confirmed [44].

The percentage of women among patients with perforated duodenal ulcer throughout the 45 years of the study increased almost threefold (from 12.3 to 32.3%). This observation cannot be explained only by the longer lifespan

of women. In our study an average expected lifespan for both gender groups has increased. In Poland, the expected lifespan for men was about 67 years for the first study period and reached 71 for the last (almost 6% increase). In the group of Polish women, mean lifespan also increased—from almost 75 years for the first study period to almost 80 years for the last one (about a 6% increase). Differences in lifespan between men and women did not, however, prove significant. Therefore the increasing prevalence of ulcer disease in elderly women does not reflect the longer lifespan of women.

For almost half a century there was an increase in the proportion of women with perforated duodenal ulcer observed in our study. Thus for such localization of perforation, the male to female ratio changed from about 7:1 to slightly more than 2:1. Similar observations were also found in other studies [6, 15, 19], but still others did not reveal such results [13, 17, 18].

According to our data, the mean age of women with perforated stomach ulcer did not differ significantly from women with perforation of duodenal ulcer. Their mean age was also similar to the mean age of male patients with perforated stomach ulcer. Only men with perforated duodenal ulcer presented with significantly lower mean age as compared to the above mentioned groups. Similar differences were observed in the study from England that found the mean age of women with perforated duodenal ulcer to be 10 years higher than the mean age of men [15]. However, that study presented a markedly older population than ours, with the mean age of male patients of 67.6 years and that of female patients of 77.6 years [39]. Most of the recent studies revealed a marked increase in the mean age of patients admitted to the hospital for complications of peptic ulcer disease, including perforations [5, 15, 17–19]. Similar results, although without statistical significance, were found in our material.

The introduction of more and more potent anti-ulcer drugs, including eradication of *H. pylori*, proved effective enough to decrease the number of patients hospitalized and treated for uncomplicated peptic ulcer disease. At present, only patients presenting with complications are treated surgically [1, 30, 32, 46, 47]. It is, however, believed that—in the general population—modern treatment of peptic ulcer disease did not cause the significant decrease in the number of complications [34, 46, 47]. Such a statement can, however, be revised, because recent studies from Spain, Sweden, Italy, and Taiwan indicate that from the time of introduction of PPIs the number of perforations markedly decreased [6, 16, 18, 25].

In summary, it is possible to state that divergence between results of the studies on the incidence, characteristics of patients, and localization of perforated ulcer are related to the multifactorial pathogenesis of this

complication of peptic disease, including regional differences of dietary customs, smoking habits, and prevalence of the use of NSAIDs.

Conclusions

The percentage of women with perforated duodenal ulcer continuously and statistically significantly rises. Men with perforated duodenal ulcer were significantly younger than women with this complication and than patients with perforated stomach ulcer regardless of gender. Mean ages of male and female patients with perforated duodenal ulcer over the last 45 years showed an insignificant upward trend.

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